gulonic acid starting compound" of step (b) and "2-keto-L-gulonic acid compound" of step (e). Similarly, "starting material" has been substituted for the term "2-keto-L-gulonic acid" in claims 25 and 26, for the terms "synthesis of L-ascorbic acid from 2-keto-L-gulonic acid" in claim 27, and for the term "synthesis" in claims 28 and 29. Support for these changes are found in the specification generally and in claim 19 as originally filed. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version With Markings to Show Changes".

Rejection of Claims 19-57 under 35 U.S.C. §103(a)

Claims 19-57 are rejected under 35 U.S.C. §103(a) in view of the disclosure of Wedzicha et al. *Adv. Exp. Med. Biol.* **1991**, 289, 217-36 ("Wedzicha"); the disclosure of Reichstein, U.S Patent No. 2,265,121 ("Reichstein") in view of Hinkley et al., U.S. Patent No. 3,721,663 ("Hinkley"); Reichstein in view of Hinkley and Wedzicha; and Reichstein in view of Wedzicha. Applicants respectfully traverse the rejection and the statements made in support thereof.

The present invention is a continuous process for manufacturing L-ascorbic acid comprising the steps of (a) heating an aqueous solution of a starting material comprising 2-keto-L-gulonic acid or a derivative of 2-keto-L-gulonic acid in a reactor in the presence of at least one sulfite species under conditions such that L-ascorbic acid is generated; (b) continuously removing from the reactor a post-reaction solution comprising unreacted starting material and L-ascorbic acid; (c) removing at least a portion of sulfur containing compounds from the post-reaction solution; (d) removing at least a portion of the L-ascorbic acid from the post reaction solution; and (e) recycling unreacted starting material back to the reactor (claim 19 as amended). The presence of the sulfite species in the reaction mixture provides an ascorbic acid product with reduced color.

The primary reference cited by the Examiner, Wedzicha, discusses the mechanism by which sulfites inhibit anaerobic and oxidative browning of ascorbic acid in food materials. Wedzicha would not have taught or suggested the present invention and would not have provided a reasonable expectation that Applicants' invention would

succeed. Applicants respectfully submit that a proper analysis of the present invention and the disclosure of Wedzicha would consider at least 3 important and distinct differences.

First, the Wedzicha disclosure discusses sulfite inhibition only of ascorbic acid browning and of the Maillard reaction. By contrast, the present invention uses sulfites to reduce color derived from the many compounds that are present in a chemical process to produce ascorbic acid. Such compounds may include, for example, 2-keto-L-gulonic acid (abbreviated herein as "KLG"), derivatives of KLG, and the various intermediate reaction products, reaction by-products, and decomposition products of KLG and ascorbic acid. Outside of ascorbic acid, the Wedzicha disclosure does not address any of these compounds or related materials, their color forming properties, or of the reduction of color in the presence of sulfites. With such limited scope, therefore, the Wedzicha disclosure could not have reasonably taught or suggested Applicants' invention to one of ordinary skill in the art.

Second, Wedzicha discusses inhibition of ascorbic browning only in food materials and is absolutely silent on the reduction of color in a chemical process. These two environments differ drastically in important chemical and physical properties such temperature, pressure, concentration, solvent, and, as noted above, the nature of the reactive chemical species that are present. These variables add to the unpredictability of an already complex and uncertain chemistry. Wedzicha states, for example, "The oxidative browning of ascorbic acid is inhibited by S(IV) though the mechanism of its inhibition is unknown" (page 230, paragraph 5). Because of these differences, Applicants submit that no reasonable prediction on the effectiveness of sulfites for reducing color in Applicants' ascorbic acid process could have been made at the time of invention based on the teachings of Wedzicha.

Finally, the effectiveness of sulfites for reducing ascorbic acid color is not, by any means, conclusive from the Wedzicha disclosure. Wedzicha states that "color formation is only delayed by S(IV)" (page 230, paragraph 2). Thus, from this statement and the differences noted above, it would be entirely reasonable for a person of ordinary skill in the art to conclude that the presence of sulfites would not be effective for reducing color of ascorbic acid in a continuous chemical process, especially at elevated temperatures.

Given the problem faced by the Applicants, the differences in chemical species and physical environments, and the questionable effectiveness of sulfites for color reduction, a person of ordinary skill in the art simply would not have looked to Wedzicha for a teaching, suggestion, or motivation to produce the claimed invention.

Claims 19-57 stand rejected over the disclosure of Reichstein in view of Hinkley. Reichstein teaches a process for preparation of ascorbic acid by lactonization of 2-keto-L-gulonic acid and 2-keto-L-gulonic derivatives in the presence of acid catalysts. Reichstein would not have taught or suggested Applicants' process. In particular, Reichstein would not have taught or suggested (1) a continuous process for ascorbic acid; (2) the presence of sulfites to reduce color; and (3) the continuous separation L-ascorbic acid product, sulfur-containing compounds, and 2-keto-L-gulonic acid from the reaction product. In addition, Reichstein would not have taught or suggested a continuous recycle of the recovered 2-keto-L-gulonic acid to the reaction mixture. Without a teaching or suggestion of these features, Applicants respectfully submit that the stated rejection is not supported by the disclosure of Reichstein.

The disclosure of Hinkley adds little to remedy the shortcomings of Reichstein. Although aqueous SO_2 is disclosed as an acid catalyst to accomplish simultaneous hydrolysis and lactonization of glycosidic acids to form ascorbic acids, Hinkley, either alone or in combination with Reichstein, would not have taught, directed or motivated one of ordinary skill in the art to produce the claimed invention as the Office Action asserts. In fact, Hinkley points away from SO_2 as a preferred catalyst for the hydrolysis and lactonization of glycosidic acids to ascorbic acids. The Examiner is directed to the following statement from the Hinkley disclosure:

> For the obtention of maximum yields of ascorbic acid, it is preferred to effect the hydrolysis by heating the glycosidic acid in concentrated hydrochloric acid at a temperature of 70-90°C for sufficient time to complete the hydrolysis. [Hinkley, column 3, lines 57-61]

Based on the above, one of ordinary skill in the art would have been motivated to select concentrated HCl as the preferred catalyst instead of SO_2. In addition, Hinkley and Reichstein would not have taught or suggested the presence of sulfites, including SO_2, in a reaction mixture to reduce the color of the ascorbic acid product. Finally, Reichstein

and Hinkley, alone or in any reasonable combination, would not have taught or suggested Applicants' five-step, continuous process for ascorbic acid.

Claims 19-57 also stand rejected under 35 U.S.C. §103(a) over the disclosure of Reichstein, in view of Hinkley and Wedzicha. The shortcomings of the combination of Reichstein and Hinkley in rendering the present invention obvious are set forth above and incorporated herein by reference. The addition of the disclosure of Wedzicha fails to cure these shortcomings. As noted previously, Wedzicha discusses only inhibition of browning by ascorbic acid present in food and is silent on the use of sulfites in a process for the preparation of ascorbic acid from 2-keto-L-gulonic acid or derivatives thereof. Thus, the combination of Reichstein, Hinkley, and Wedzicha provides no additional teaching, suggestion, or motivation that would have directed one of ordinary skill in the art to produce Applicants' process as claimed.

The Examiner rejected claims 19-57 under 35 U.S.C. §103(a) over the disclosure of Reichstein in view of Wedzicha. The arguments set forth above traversing the combination of Reichstein and Hinkley and the combination of Reichstein, Hinkley and Wedzicha are incorporated herein by reference. Applicants respectfully submit that the combination of the disclosures of Reichstein, Hinkley, and Wedzicha also fail to teach or suggest the present invention for the reasons delineated above.

Applicants respectfully submit that the stated rejection fails to establish a *prima facie* case of obviousness. The teachings of Wedzicha, Hinkley, and Reichstein, either individually or in any reasonable combination, (1) would not have taught or suggested the Applicants' continuous, 5-step process for the preparation of ascorbic acid nor would have provided any suggestion to combine or modify references in a way to arrive at the presently claimed invention; (2) would not have provided motivation for the use of sulfites in a process to prepare an ascorbic acid with reduced color; and (3) would not have provided a reasonable expectation of success because of the lack of a suggestion or teaching of the embodiments or specific limitations of Applicants' process. Applicants, therefore, respectfully request reconsideration of the application and withdrawal of the rejection.

Applicants' believe that each of the arguments given in the Office Action have been addressed and that the references relied upon, either separately or in

combination, do not support rejection of the claims under 35 U.S.C. §103(a). Accordingly, the withdrawal of the rejections and allowance of the application are earnestly solicited.

Respectfully submitted,

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January 21, 2003
Date

CERTIFICATE OF MAILING UNDER 37 CFR 1.8(a)

I hereby certify that this paper (along with any referred to as being attached or enclosed) is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

Cathy L. Adkins

1/22/03
Date

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims

19. (Amended) A continuous process for manufacturing L-ascorbic acid comprising the steps of:

(a) heating an aqueous solution of a starting material comprising 2-keto-L-gulonic acid or a derivative of 2-keto-L-gulonic acid in a reactor in the presence of at least one sulfite species under conditions such that L-ascorbic acid is generated;

(b) continuously removing from the reactor a post-reaction solution comprising unreacted ~~2-keto-L-gulonic acid~~ starting ~~compound~~ material and L-ascorbic acid;

(c) removing at least a portion of sulfur containing compounds from the post-reaction solution;

(d) removing at least a portion of the L-ascorbic acid from the post reaction solution; and

(e) recycling unreacted ~~2-keto-L-gulonic acid compound~~ starting material back to the reactor.

25. (Amended) The method of claim 19, wherein the ~~2-keto-L-gulonic acid~~ starting material comprises an aqueous solution from a fermentation process for producing 2-keto-L-gulonic acid.

26. (Amended) The method of claim 19, wherein the ~~2-keto-L-gulonic acid~~ starting material comprises an aqueous solution of 2-keto-L-gulonic acid derived from the hydrolysis of the bisacetonide of 2-keto-L-gulonic acid or the esters of 2-keto-L-gulonic acid.

27. (Amended) The method of claim 19, wherein the ~~synthesis of L-ascorbic acid from 2-keto-L-gulonic acid~~ starting material comprises an aqueous solution of 1 to 40 weight percent 2-keto-L-gulonic acid.

28. (Amended) The method of claim 19, wherein the ~~synthesis~~ starting material comprises an aqueous solution of 5 to 30 weight percent 2-keto-L-gulonic acid.

29. (Amended) The method of claim 19, wherein the ~~synthesis~~ starting material comprises an aqueous solution of 8 to 15 weight percent 2-keto-L-gulonic acid.